REMARKS

Claims 8-11 and 16-36 are pending. Claims 16-36 are directed to the elected subject matter and are under active examination. Claims 8-11 are withdrawn from consideration. Favorable reconsideration is respectfully requested.

The present invention relates to acellular compositions which contain, *inter alia*, an isolated protective antigen (PA) from *B. anthracis* and killed spores obtained from specified mutant strains of *B. anthracis*. See independent Claims 16, 22, 27 and 32.

The present Inventors have unexpectedly discovered that the use of ***killed spores*** (which may be purified or unpurified) in combination with the protective antigen provides a composition having a strong protective capacity, which is clearly greater than that obtained with the protective antigen or the killed spores alone, as shown by the Examples of the present application.

As a result, the present invention provides an immunogenic composition or a vaccine which has strong protective action, a simple vaccination protocol and minimum side effects.

The rejection of the claims under 35 U.S.C. §103(a) over Kraevets et al., Derwent abstract only, is respectfully traversed. Kraevets et al. fail to suggest the claimed compositions.

Kraevets et al. disclose immunogenic compositions or vaccines containing a protective antigen and a ***live strain*** of *B. anthracis* which lacks the capsule (i.e., lack of pX02). The reference fails to describe the use of killed spores of *B. anthracis*.

One skilled in the art would not be motivated to use killed spores to obtain the claimed compositions. This is because killed microorganisms are usually used when the attenuation of the microorganism is difficult to obtain. However, killed microorganisms generally provide less effective protection. It is known in the art that attenuation of *B. anthracis* is well-documented. Therefore, there is no motivation to use killed spores of *B.*

anthracis. In addition, one reading Kraevets et al. would not have predicted that the claimed composition containing killed spores would have the unexpected properties of strong protective capacity, complete immunization with a single injection (animals) or two injections (humans) with minimal side effects. This is because the reference fails to even mention the use of killed spores at all.

Based on the foregoing, Claims 16-36 are not obvious over Kraevets et al. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejections of the claims under 35 U.S.C. §112, first paragraph, is believed to be obviated by the amendment submitted above in part and is in part respectfully traversed.

Regarding the biological materials, Applicants confirm that materials have been deposited under the terms of the Budapest Treaty. Applicants confirm that the deposit has been accepted by an International Depository Authority under the Treaty, that all restrictions upon public access to the deposited material will be removed upon the grant of a patent from the present application, and that the deposited materials will be replaced if viable samples of the material cannot be dispensed by the depository.

Regarding enablement, any strain may be used in the present invention, provided that the following two conditions are met:

(1) the strain is in the form of killed spores and

(2) the skilled spores are associated with an anthrax protective antigen.

An immunogenic composition meeting these conditions has an unexpected synergistic activity and has a strong protective action; moreover it allows a simple vaccination protocol and minimum side effects.

In fact, the following may be deduced from Pezard et al.:

- pXO1 may be important in the survival of *B. anthracis* in a host (page 1369, right column, last line)

- the different mutants analyzed in Pezard et al. have the following properties (see also figure 1 of Pezard et al.):

RP8:	PA^-	EF^+	LF^+
RP9:	PA+	EF-	LF+
RP10:	PA+	EF+	LF-
RP40:	PA+	EF-	LF-
RP4:	PA-	EF-	LF+
RP31:	PA-	EF+	LF-

From those results:

* all the strains producing PA (RP42, RP10 and RP9) elicited high levels of specific antibodies against PA,

* Mutants producing EF (RP31), LF (RP4) or EF and LF (RP8) elicited a weak and low specific antibody response,

* Strains producing EF or LF and PA elicited a stronger LF or EF response,

* Titers of antibodies to EF and LF were significantly higher in animals immunized with bacteria also producing PA, and

* pXO1 may have a role in the survival of bacteria in the host.

Therefore, contrary to the affirmations of the Examiner, there is no link between the properties of the killed spores and results relating to living spores as regards to evaluation of the properties of immunogenic compositions containing killed spores. The same applies for the other documents cited by the Examiner (i.e., Ivins et al.).

In view of the foregoing, withdrawal of these grounds of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, second paragraph, is believed to be obviated by the amendment submitted above in part and is in part respectfully traversed.

Regarding the optional purification of the killed spores, considering that live spores have been used without any purification, it is not required to purify the killed spores in the present invention. It is well-known that when a virulent microorganism is killed by exposure to a chemical such as formaldehyde, it can be used as such in a vaccine. Therefore, there is no requirement for purification.

In view of the foregoing, the claims are definite within the meaning of 35 U.S.C. §112, second paragraph. Therefore, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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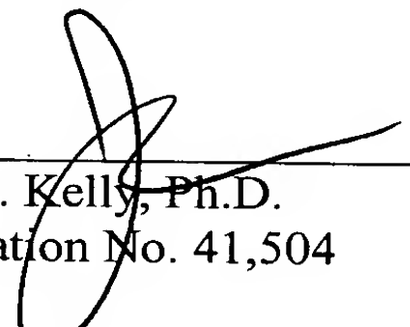

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